a plurality of second-strand sequencing reads, wherein the plurality of first-strand sequencing reads and the plurality of second-strand sequencing reads each comprise a bar code sequence and a sequence from a circulating nucleic acid molecule;

(e) grouping sequencing reads based on (i) the bar code sequence and (ii) sequence information from the circulating nucleic acid molecule, wherein a group comprises sequencing reads from the cypher-target amplification products of one of the cypher-target nucleic acid complexes;

(f) comparing the first-strand sequencing reads with the second-strand sequencing reads within the groups, and generating error-corrected sequences of the circulating nucleic acid molecules by distinguishing erroneous nucleotides in one strand that lack a matched base change in the complementary strand;

(g) providing a reference sequence, said reference sequence comprising one or more loci;

(h) mapping error-corrected sequences to a given locus of the one or more loci; and

(i) quantifying the error-corrected sequences that map to the given locus that comprise a cancer biomarker, wherein the cancer biomarker comprises mutation of a single nucleotide.

40. The method of claim **39**, wherein the quantifying comprises determining a copy number of the cancer biomarker.

41. The method of claim **39**, wherein the plurality of circulating nucleic acid molecules comprise a mutation present at a frequency of 2.1×10^{-6} or lower.

42. The method of claim **39**, wherein generating the error-corrected sequences results in a measureable sequencing error rate from about 10^{-6} to about 10^{-8}.

43. The method of claim **39**, wherein the plurality of first-strand sequencing reads and the plurality of second-strand sequencing reads are filtered based on assigned quality scores.

44. The method of claim **39**, wherein the circulating nucleic acid molecules comprise plasma DNA biomarkers.

45. The method of claim **39**, further comprising detecting a stage of cancer in the patient.

46. The method of claim **39**, further comprising assessing response to cancer therapy in the patient based on the cancer biomarker.

47. The method of claim **39**, wherein the cancer biomarker is a mutation that confers resistance to therapy.

48. The method of claim **39**, wherein the patient sample comprises a blood sample.

49. The method of claim **39**, wherein the circulating nucleic acid molecules are obtained from plasma.

50. The method of claim **39**, wherein the circulating nucleic acid molecules are derived from cancer cells.

51. The method of claim **39**, wherein the circulating nucleic acid molecules are double-stranded DNA molecules.

52. The method of claim **39**, wherein the ligating comprises ligating to an overhang or a blunt end.

53. The method of claim **39**, wherein the cypher polynucleotides comprising the bar codes are contained within a pool of cypher polynucleotides comprising known sequences.

54. The method of claim **39**, wherein the bar codes are double-stranded DNA sequences.

55. The method of claim **39**, further comprising purifying a plurality of cypher-target nucleic acid complexes prior to sequencing, wherein the purified cypher-target nucleic acid complexes comprise nucleic acid molecules from specific genomic regions.

56. The method of claim **39**, further comprising purifying a plurality of cypher-target nucleic acid complexes prior to sequencing, wherein the purified cypher-target nucleic acid complexes comprise specific nucleic acid molecules that map to specific genomic regions.

57. The method of claim **39**, wherein grouping sequencing reads is based on (i) the bar code sequence and (ii) sequence information from an end of the circulating nucleic acid molecule.

58. The method of claim **39**, wherein the ligating comprises ligating bar codes to both ends of the circulating nucleic acid molecules.

59. The method of claim **58**, wherein the bar codes at both ends together form a unique pair of identifiers that differ between each of the other pairs of identifiers ligated to the circulating nucleic acid molecules.

60. The method of claim **39**, wherein the reference sequence is from a non-tumor tissue.

61. The method of claim **39**, wherein the reference sequence is a human genomic sequence.

62. The method of claim **39**, wherein the quantifying comprises calculating the frequency of circulating nucleic acid molecules comprising the single nucleotide mutation in the plurality of circulating nucleic acid molecules.

63. The method of claim **39**, wherein the circulating nucleic acid molecules are double-stranded DNA molecules, and wherein for each of a plurality of groups of sequencing reads, step (f) comprises comparing the first-strand sequencing reads with the second-strand sequencing reads to form an error-corrected sequence, wherein the error-corrected sequence comprises only nucleotide bases at which the first-strand sequencing reads and second-strand sequencing reads are in agreement, such that the single nucleotide mutation is identified as a true mutation.

64. The method of claim **39**, further comprising detecting a transition mutation, a nucleic acid chemical damage, a rare mutant, a quantity of virus, nucleic acid heterogeneity, somatic mutations, viral mutations, tumor heterogeneity, mitochondrial mutations, a tumor cell, a mutator phenotype, a cancer, or a mutation frequency.

65. The method of claim **39**, wherein the bar code sequences comprise random or partially random sequences.

66. The method of claim **39**, wherein the bar code sequences comprise nonrandom sequences.

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